EXHIBIT C

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent:

Patent No.	:	5,811,447	)
Atty. Dkt.	:	32286-323242	)
Inventors	:	Kunz *et al.*	)
Assignee	:	Boston Scientific Scimed, Inc.	)
			)
Issued	:	September 22, 1998	)
Title	:	THERAPEUTIC INHIBITOR OF VASCULAR SMOOTH MUSCLE CELLS	)
			)
			)

Mail Stop: Hatch-Waxman PTE
Commissioner for Patents
P.O. Box 1450
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REQUEST FOR RECONSIDERATION OF DENIAL OF PATENT TERM EXTENSION APPLICATION UNDER 35 U.S.C. § 156 FOR U.S. PATENT NO. 5,811,447

AND

REQUEST FOR GRANT OF PATENT TERM EXTENSION UNDER 35 U.S.C. § 156 FOR U.S. PATENT NO. 5,811,447

AND

REQUEST FOR INTERIM PATENT EXTENSION FOR U.S. PATENT NO. 5,811,447

Dear Commissioner:

Angiotech Pharmaceuticals Inc. (Angiotech or Applicant), hereby respectfully requests Reconsideration under 37 CFR §1.750 of the U.S. Patent and Trademark Office (USPTO) Denial Of Patent Term Extension Application Under 35 U.S.C. §156 For U.S. Patent No. 5,811,447 mailed October 16, 2015 (Denial). Applicant respectfully requests that:

1) The decision denying Patent Term Extension be REVERSED;

2) Patent Term Extension be GRANTED; and

3) An additional Interim Patent Term Extension be GRANTED for U.S. Patent No. 5,811,447 until such time as the Patent Term Extension is granted or Applicant's available remedies are exhausted.

The Denial should be reversed, because it is based on the USPTO's incorrect determination that U.S. Patent Number 5,811,447 (the '447 Patent) does not claim a method of using the ZILVER® PTX® Drug Eluting Peripheral Stent (ZILVER controlled-delivery system), the product subject to regulatory review under PMA P1000022.

Applicant should be granted Patent Term Extension (PTE) because the '447 Patent claims a method of using the ZILVER controlled-delivery system in view of applicable statutory and case law.

Interim Patent Term Extension of the '447 Patent should be granted in order to prevent patent expiration until a final decision is reached.

BACKGROUND

The Food and Drug Administration (FDA) granted a Pre-Market Approval application (PMA) for the ZILVER controlled-delivery system on November 15, 2012 pursuant to Section 515 of the Federal Food, Drug and Cosmetic Act (21 U.S.C. §360(e)). The '447 Patent was granted on September 22, 1998 and includes 18 claims, of which at least claim 12 reads on methods of using the ZILVER controlled-delivery system in the manner approved by the FDA.

Applicant timely filed its PTE Application for the '447 Patent on December 7, 2012 and a supplement on February 28, 2013.

On March 23, 2015, the USPTO sent a Requirement for Information to Applicant seeking additional information. Applicant timely responded on June 19, 2015.

On May 11, 2015, the FDA indicated that the ZILVER controlled-delivery system had been subject to regulatory review and confirmed that approval represented the first permitted commercial marketing or use.

On June 19, 2015, Applicant filed a Request for Interim Extension under 35 U.S.C. §156(e)(2) and 37 C.F.R. §1.760 for one year. On September 17, 2015, the USPTO granted the Request for only a period of three months from the original expiration date of the '447 Patent.

On October 16, 2015, the USPTO issued a Denial Of Patent Term Extension Application Under 35 U.S.C. § 156 for U.S. Patent No. 5,811,447. During a follow-up call, the USPTO informed Applicant that in view of the Denial, the USPTO did not plan to grant any further Interim Extension.

In the absence of further action, the '447 Patent will expire on December 22, 2015.

The '447 Patent

The '447 Patent issued on September 22, 1998 from U.S. Serial No. 08/450,793. Claim 12 of the '447 Patent recites:

> 12. A method for biologically stenting a mammalian blood vessel, which method comprises administering to the blood vessel of a mammal a cytoskeletal inhibitor in an amount and for a period of time effective to inhibit the contraction or migration of the vascular smooth muscle cells.

Claim 12 pertains to a defined method "for biologically stenting a mammalian blood vessel." This method requires:

-"administering to the blood vessel of a mammal a cytoskeletal inhibitor"

-"in an amount"

-"and for a period of time"

-"effective to inhibit the contraction or migration of the vascular smooth muscle cells."

Claim 12 does not encompass any and all possible methods of "biological stenting."

Persons of skill in the art appreciate that local administration of an antirestenotic drug directly to the blood vessel wall allows for the blood vessel wall to receive a high and sustained concentration of the drug without burdening the entire body of the patient with the drug and resultant undesirable side effects of systemic administration ("[heparin] reportedly inhibits smooth cell proliferation in vitro but when used in vivo has the potential adverse side effect of inhibiting coagulation" ('447 Patent, col. 1, lines 60-64); see also, A.Schömig et al., "Prevention of Restenosis by Systemic Drug Therapy: Back to the Future?", Circulation, 112 (2005) 2759-2761; S.J.Sollott et al., "Taxol Inhibits Neointimal Smooth Muscle Cell Accumulation after Angioplasty in the Rat", J. Clin. Investigation, 95 (1995) 1869-1876).

It is clear from the written description of the '447 Patent that claim 12 encompasses the local administration of drugs to the blood vessel wall (e.g., "inhibitory agents may have systemic toxicity that could create an unacceptable level of risk for patients with cardiovascular disease" (col. 2, lines 19-22); "[l]ocal administration of such sustained release compounds would also be useful in the treatment of other conditions" (col. 2, lines 56-59); local administration is "designed to reduce systemic toxicity while providing a high level of exposure for the target smooth muscle

cells" (col 54, lines 41-46)"; "[t]he therapeutic agent may be targeted, but is preferably administered directly to the traumatized vessel" (col. 36, lines 43-45); "a sustained exposure of the vessel to the therapeutic agent is preferable in order to maximize these anti-migratory effects [on vascular smooth muscle cells]" (col. 36, lines 52-54)).

Furthermore, the written description of the '447 Patent clearly contemplates that the invention of claim 12 encompasses the local and sustained administration of the cytoskeletal inhibitor in conjunction with a physical angioplasty procedure that can include the placement of a physical stent. ("The therapeutic agent may be targeted, but is preferably administered directly to the traumatized vessel following the angioplasty or other traumatic event" (col. 36, lines 43-45); "Balloon traumatized pig arteries that had been treated with cytochalasin B displayed a larger luminal area at the 4 day and 3 week post-treatment time points" (col. 69, lines 22-24); "[A] therapeutically effective dosage of a therapeutic conjugate or dosage is useful in treating vascular trauma resulting from disease ... or vascular surgical procedures such as angioplasty, atheroectomy, placement of a stent (e.g., in a vessel)" (col. 30, lines 39-43)).

The ZILVER® PTX® Drug Eluting Peripheral Stent

The ZILVER® PTX® Drug Eluting Peripheral Stent (ZILVER controlled-delivery system) received pre-market regulatory approval on November 15, 2012. As acknowledged by the FDA, this represented the first permitted commercial marketing or use. Accordingly, the approval of the ZILVER controlled-delivery system can be the basis of PTE.

The ZILVER controlled-delivery system is a product that provides, among other things, local, controlled release of paclitaxel, and as such can be considered a controlled-delivery

system, in addition to having physical stenting characteristics.[1] The ZILVER controlled-delivery system provides continued biological stenting through locally directed, sustained release of its paclitaxel coating to maintain the dilation of the blood vessel wall achieved through angioplasty. This is shown in the Summary of Safety and Effectiveness Data (SSED) of the U.S. Food & Drug Administration (FDA) approval package for the ZILVER controlled-delivery system, which indicates the following:

(a) The ZILVER controlled-delivery system is an implantable blood-contacting device (SSED, p. 8 (sec. IX.A.) top bridging para.);

(b) The ZILVER controlled-delivery system is for improving luminal diameter for the treatment of de novo or restenotic symptomatic lesions in vascular disease of arteries (SSED, p. 1 (sec. II));

(c) The ZILVER controlled-delivery system is coated with the drug paclitaxel (SSED, p. 2 (sec. V), para. 1);

(d) Paclitaxel prevents the smooth muscle cell proliferation and migration known to occur during the restenotic process in arteries (SSED, p. 4 (sec. V), para. 1); and

(e) The primary patency rate at 12 months was 90.2% for the ZILVER controlled-delivery system, greater than the 72.9% for the bare Zilver stent, and demonstrating a significant drug effect in reducing restenosis with ZILVER controlled-delivery system as compared to the bare Zilver stent (SSED, p.37 (sec. X.D.2) para. 1-2).

The drug delivery benefit of the ZILVER controlled-delivery system results in its being

[1] During regulatory approval, the ZILVER® PTX® Drug Eluting Peripheral Stent (ZILVER controlled-delivery system) was compared to its "bare", i.e. uncoated, counterpart the Zilver Vascular Stent, which provides only physical stenting.

significantly more effective in maintaining primary patency than stenting with the same bare (uncoated) stent.

As shown in points (b)-(e), above, the SSED indicate that the ZILVER controlled-delivery system provides a "method for biologically stenting a mammalian blood vessel." Points (a), (c), and (d) indicate that the ZILVER controlled-delivery system "administer[s] to the blood vessel of a mammal a cytoskeletal inhibitor." Points (c)-(e) indicate that the administration of paclitaxel (the cytoskeletal inhibitor) is "in an amount and for a period of time effective to inhibit the contraction or migration of the vascular smooth muscle cells." Thus, the ZILVER controlled-delivery system can be used in "[a] method for biologically stenting a mammalian blood vessel."

THE DENIAL OF PATENT TERM EXTENSION OF THE '447 PATENT SHOULD BE REVERSED AND PATENT TERM EXTENSION OF THE '447 PATENT SHOULD BE GRANTED

Extension of the term of a patent (Patent Term Extension (PTE)) is authorized by 35 U.S.C. §156, which states the following:

> (a) The term of a patent which claims a product, a method of using a product, or a method of manufacturing a product shall be extended in accordance with this section from the original expiration date of the patent ... if-
> ...
> (4) the product has been subject to a regulatory review period before its commercial marketing or use.

1. Claim 12 of the '447 Patent is a Method of Using the ZILVER Controlled-Delivery System.

Applicant submits that claim 12 of the '447 Patent is "a method of using a product" under

35 U.S.C. §156, the product being the ZILVER controlled-delivery system.

Claim 12 of the '447 patent recites:

> 12. A method for biologically stenting a mammalian blood vessel, which method comprises administering to the blood vessel of a mammal a cytoskeletal inhibitor in an amount and for a period of time effective to inhibit the contraction or migration of the vascular smooth muscle cells.

Accordingly, the claimed method requires "biologically stenting a mammalian blood vessel" by:

-"administering to the blood vessel of a mammal a cytoskeletal inhibitor"
-"in an amount"
-"and for a period of time"
-"effective to inhibit the contraction or migration of the vascular smooth muscle cells."

As shown in the above description of the ZILVER controlled-delivery system, the SSED establishes that:

- The ZILVER controlled-delivery system provides a "method for biologically stenting a mammalian blood vessel" (See points (b)-(e), above).
- The ZILVER controlled-delivery system "administer[s] to the blood vessel of a mammal a cytoskeletal inhibitor" (See points (a), (c), and (d), above).
- Administration of paclitaxel (the cytoskeletal inhibitor) by the ZILVER controlled-delivery system is "in an amount and for a period of time effective to inhibit the contraction or migration of the vascular smooth muscle cells" (See points (c)-(e), above).

Thus, the ZILVER controlled-delivery system is used in "[a] method for biologically stenting a mammalian blood vessel" as required by claim 12.

In the Denial, the USPTO inappropriately ignores paclitaxel administration and solely focuses on the structural features of the ZILVER controlled-delivery system, stating "the claimed

method must recite one or more structural elements." (Denial, p. 4.) The USPTO points to no authority that requires that, to be eligible for PTE, a method claim must include structural elements of the approved device. All that is required is that the patent claim a method of using the device. As set forth above, the '447 Patent is directed to a method of using the ZILVER controlled-delivery system, so the Denial must be reversed.

Furthermore, the USPTO ignores the drug delivery features of the ZILVER controlled-delivery system, asserting that:

> [P]atency [using the ZILVER controlled-delivery system] is achieved whether or not a cytoskeletal inhibitor (paclitaxel) is included in the stent system. But in the '447 patent, patency is achieved by the pharmaceutical agent alone (*i.e.*, 'biological stenting['']), rather than by a physical stent

(Denial, pages 6-7). The USPTO's statement that the '447 Patent precludes using a physical stent in conjunction with the "biological stenting" claim is incorrect and further delineates the narrow view taken by the USPTO and the inappropriate denial of PTE. Claim 12 of the '447 Patent is a "method comprising administering to the blood vessel of a mammal a cytoskeletal inhibitor . . ." Comprising indicates that other steps may be included. Thus, there is nothing that precludes achieving biological stenting in conjunction with physical stenting. The bare Zilver stent, to which the ZILVER controlled-delivery system was compared during regulatory review, achieves only physical stenting. The ZILVER controlled-delivery system improves on this by also providing biological stenting, thus meeting the requirements of claim 12 of the '447 Patent.[2] For this reason as well, the '447 patent is directed to a method of using ZILVER controlled-delivery system and the Denial must be reversed.

[2]The primary patency rate at 12 months for the ZILVER® PTX® Drug Eluting Peripheral Stent (ZILVER controlled-delivery system) is 90.2%, greater than the 72.9% for the bare Zilver stent.

For at least the reasons of record and those set forth above, through claim 12, the '447 Patent "claims ... a method of using a product", the product being the ZILVER controlled-delivery system that was subject to a regulatory review period before its commercial marketing or use, as required by 35 USC §156, and Patent Term Extension should be granted.

2. Reliance on the Hoechst-Roussel Pharmaceuticals Case Is Misplaced.

The Denial relies on the decision of the Federal Circuit in *Hoechst-Roussel Pharmaceuticals Inc. v. Lehman*, 109 F.3d 756, 42 U.S.P.Q.2d 1220 (Fed. Cir. 1997) (Hoechst). However, the relevant facts of the present case are different, so that Hoechst is inapplicable.

The USPTO cites to page 759 of Hoechst for the proposition that "the concept of a 'claim' is different from the concept of infringement, and, as a result, the plain meaning of 'claims' is not the same as the plain meaning of infringement." The Denial then states that "Applicant has conflated the concept of claiming a method of using the product (the medical device which was subject to regulatory review) with whether making, using, offering to sell, or selling the ZILVER® PTX Drug Eluting Peripheral Stent would, in theory, infringe claim 12 of the '447 patent."

Applicant has not "conflated" concepts in any such way. Claim 12 of the '447 patent is directed to "administering to the blood vessel of a mammal a cytoskeletal inhibitor." This is precisely the method carried out with the ZILVER controlled-delivery system. Contrary to the assertion in the Denial, Applicant is not relying on the fact that use of the ZILVER controlled-delivery system infringes claim 12 to establish eligibility for PTE.

As set forth above, claim 12 of the '447 Patent clearly encompasses a method of using

the ZILVER controlled-delivery system to biologically stent a mammalian blood vessel. That is, the method using the ZILVER controlled-delivery system is a "method for biologically stenting a mammalian blood vessel" encompassed by claim 12. This is what is required by the statute and relied upon by the Applicant.

The facts in Hoechst were entirely different than the present facts. Hoechst's 4,631,286 patent claimed the compound 1-hydroxy-tacrine (HO-T) and a method of treating a patient with HO-T. Hoechst requested Patent Term Extension of its patent based on the regulatory review period of Warner-Lambert's product COGNEX®, of which the active ingredient was tacrine hydrochloride (T-HCl). The USPTO then denied Hoechst's application for PTE of its patent for two reasons: (i) Hoechst was not a proper PTE applicant, because it was not involved in the regulatory approval process; and (ii) Hoechst's patent did not claim T-HCl. The majority opinion by Judge Clevenger affirmed the denial of Hoechst's request for PTE on the basis of reason (ii). Applicant observes that in her concurrence, Judge Newman affirmed the denial of Hoechst's request for PTE on the basis of reason (i) and rebuked the majority's rationale based on reason (ii). Reason (i) is irrelevant to the present situation, in which Angiotech is a proper PTE Applicant.

Reason (ii) is readily distinguishable from the present situation. Hoechst's patent simply did not claim the molecule that was subject to the regulatory approval process nor did it claim a method of administering the molecule. That is, the HO-T molecule claimed by Hoechst's patent was simply different than the T-HCl molecule and its use that was subjected to the regulatory approval process. In contrast, claim 12 of the '447 patent is directed to "administering to the blood vessel of a mammal a cytoskeletal inhibitor", which is precisely the method carried out

with the ZILVER controlled-delivery system.

Accordingly, claim 12 of the '447 Patent claims a method using the ZILVER controlled-delivery system that was subject to the regulatory approval process. Therefore, the '447 Patent should be granted the requested Patent Term Extension.

3. The USPTO Should Grant Extension of the '447 Patent to be Consistent with Its Past Practice

The fact that a patent claim reads on products in addition to the approved product cannot be the basis for denying PTE. Virtually any patent claim reads on more than one single commercial embodiment. The USPTO's past approval of PTE for a patent claiming a method of using a product demonstrates this point.

On January 30, 2001 the USPTO granted a Certificate Extending Patent Term of U.S. Patent No. 5,041,126 to C. Gianturco on the basis of the regulatory review period for the Cook GRII™ Coronary Stent. In the Application for Extension of Patent Term, the applicant, Cook Incorporated, asserted in section 8 that "[c]laim 1 [of U.S. Pat. 5,041,126] reads on the method for use of the Cook GRII™ Coronary Stent." Claim 1 as granted stated:

> 1. A method for inserting a stent which comprises:
> (a) engaging a stent, having a longitudinal length, around a balloon catheter,
> (b) locating the catheter and stent within a passageway, and
> (c) inelastically expanding the stent, while maintaining the longitudinal length of the stent, by inflating the balloon catheter within the stent to inelastically deform the stent until the stent engages the passageway.

There are a nearly infinite number of stent configurations that could meet the requirements of claim 1, far more than just the FDA-approved Cook GRII™ Coronary Stent.

Nevertheless, the USPTO granted Patent Term Extension of U.S. Pat. 5,041,126. The USPTO's grant of Patent Term Extension for U.S. Pat. 5,041,126 was proper, because claim 1 is a method of using a product that was subject to regulatory review.

In a similar manner, the USPTO should approve Patent Term Extension of the instant '447 Patent, because its claim 12 to a method of use of a product encompasses the use of the FDA-approved ZILVER controlled-delivery system.

THE USPTO SHOULD GRANT AN ADDITIONAL INTERIM PATENT TERM EXTENSION OF THE '447 PATENT

The USPTO has indicated that it will not grant any additional Interim Patent Term Extension for the '447 Patent. However, in the absence of additional Interim Patent Term Extension, the '447 Patent will expire on December 22, 2015. The statute requires that "[i]f the term of a patent for which an application has been submitted under subsection (d)(1) would expire before a certificate of extension is issued or denied under paragraph (1) respecting the application, the Director **shall** extend, until such determination is made, the term of the patent for periods of up to one year if he determines that the patent is eligible for extension." (35 U.S.C. §156(e)(2), emphasis added.)

The Denial asserts that it "is a final agency action within the meaning of 5 U.S.C. 704 for purposes of seeking judicial review." With this Request for Reconsideration, Applicant submits that a final determination of PTE has not been made and that the Denial is no longer a final agency action. Accordingly, an additional Interim Extension should be granted.

Furthermore, Applicant could be severely prejudiced if the '447 Patent were allowed to

expire before Applicant has exhausted its remedies in seeking reversal of the Denial. For this reason as well, an additional Interim Extension should be granted.

In view of the above, the USPTO should grant an additional Interim Extension for one year from the date Applicant's prior Application was filed on June 19, 2015, or Patent Term Extension is granted.

CONCLUSION

For the reasons present in the record and the additional reasons set forth herein, the decision denying Patent Term Extension should be reversed and Patent Term Extension should be granted. In addition, until such time as Patent Term Extension is granted or Applicant's available remedies are exhausted, additional Interim Patent Term Extension for U.S. Patent No. 5,811,447 should be granted.

It is not believed that any fees are required in conjunction with this submission. However, the Commissioner is hereby authorized to charge any deficiency in the fees filed herewith, asserted to be filed herewith, or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to Deposit Account number 22-0261, under Order number 32286-323242.

In the event that further information is required or the USPTO has questions, Applicant respectfully requests that the USPTO telephonically contact the undersigned at the number provided below.

Respectfully submitted,

Dated: November 16, 2015

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Electronic Acknowledgement Receipt

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Confirmation Number:	3349
Title of Invention:	THERAPEUTIC INHIBITOR OF VASCULAR SMOOTH MUSCLE CELLS
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Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Miscellaneous Incoming Letter	reqreconsid.pdf	631435 6debb685e29e92f243bd251be87ac51b19f a769a	no	15

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New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.